I.B.

The argument that a product's effects must be therapeutic or medical is also inconsistent with FDA's assertion of jurisdiction over products with cosmetic, recreational, and economic uses. Notably, the comments that contend that effects on the structure or function of the body must be therapeutic or medical and also beneficial do not claim that FDA incorrectly applied the structure-function provision to products with cosmetic, recreational, or economic uses. Instead, these comments attempt to avoid the inconsistency between their arguments and these precedents by expansively interpreting "therapeutic" and "medical" to encompass products with cosmetic, recreational, economic, and other apparently non-therapeutic purposes or effects. Moreover, these comments do not provide any rationale to support the position that products regulating weight are subject to the Act, but that nicotine-containing cigarettes and smokeless tobacco, which also affect weight regulation, are not. Instead, the comments assert that the weight control effects of cigarettes and smokeless tobacco are too minor to be subject to the Act's jurisdiction. This argument is refuted in section II.A.4., below.

The Agency rejects the legal premise that effects on the structure or function of the body must be therapeutic or beneficial. However, even if the Agency were to accept the manufacturers' legal premise, this would not change the Agency's decision with respect to cigarettes and smokeless tobacco. As noted previously, cigarettes and smokeless tobacco produce pharmacological effects on the structure and function of the body that are indistinguishable from the effects of a wide range of products regulated by FDA, including sedation, stimulation, weight loss, and sustaining addiction. These pharmacological effects are as "therapeutic" or "beneficial" as many effects currently regulated under the

Act, and would be sufficient to satisfy a requirement that products regulated as drug delivery devices have beneficial or therapeutic effects. Tobacco industry scientists have themselves argued that tobacco products provide "needed psychological benefits (increased mental alertness; anxiety reduction, coping with stress)"[17] and that "nicotine is a very remarkable beneficent drug."[18]

Indeed, if a new product with the powerful pharmacological effects of cigarettes and smokeless tobacco—sedation, stimulation, weight loss, and sustaining addiction—suddenly began to be distributed in the United States, there would be no question that the product would be subject to regulation under the Act because it "affect[s] the structure or any function of the body" within the Act's meaning. For example, the Agency has regulated gamma hydroxybutrate and gamma hydroxybutyric acid (collectively, GHB), a product intended to affect the structure or function of the body by promoting weight loss and muscle gain. The product is also used as a relaxant and sleep aid. GHB emerged as a steroid alternative after anabolic steroids became controlled substances. Very little was known about the product when GHB first entered the market because it was manufactured in clandestine laboratories (e.g., basements and kitchens), obtained from other black market sources, and usually distributed at health and sporting stores and clubs without labeling. The use of GHB as a steroid alternative and body-building aid is not "therapeutic"; nonetheless, the Agency successfully undertook regulatory actions against

[17] Robinson JH, Pritchard WS, The role of nicotine in tobacco use, *Psychopharmacology* 1992;108:397-407, at 398. *See* AR (Vol. 66 Ref. 31-1).

[18] Ellis C, Science Advisor to the BATCO Board, *The Smoking and Health Problem*, presented at the BATCO Research Conference, Southampton, England (1962), at 15. *See* AR (Vol. 15 Ref. 190).

I.B.

GHB pursuant to the Act's drug authorities. *See United States v. Wood*, Nos. 92-50512, 92-50514 (9th Cir. Oct. 21, 1993); 58 FR 33690, 33699 (Jun. 18, 1993); FDA Quarterly Activities Report, First Quarter, FY 1991 (Oct.-Dec. 1990).

3. One comment contends that the structure-function provision is limited to products that "purport to *change* the physical structure of the body."[19] The Agency disagrees. Although the provision covers products that change a structure or function of the body, it is not limited to such effects. Courts have rejected the view that section 201(g)(1)(C) requires an actual "change [in] the physical structure or function of the [ ] body." *"Pets Smellfree,"* 22 F.3d at 237. Moreover, cigarettes and smokeless tobacco do in fact change the physical structure of the body by, for example, affecting brain chemistry and electrical activity in the brain, reducing weight, and increasing the growth of nicotine receptors in the central nervous system.

4. One comment asserts that the structure-function provision "is not intended to authorize the regulation of products solely because FDA believes their use is harmful and undesirable."[20] The Agency agrees. However, if a particular product meets the statutory definition of drug or device, the fact that it is also associated with harms to health is a reasonable consideration for the Agency in deciding to regulate the product. The Act's legislative history supports this view. As noted, concern about weight loss products that escaped regulation in the 1906 Pure Food and Drug Act was an impetus for

[19] Joint Comments of the Cigarette Manufacturers, Comment (Jan. 2, 1996), vol. II, at 83 (emphasis added). *See* AR (Vol. 535 Ref. 96).

[20] Joint Comments of the Smokeless Tobacco Manufacturers, Comment (Jan. 2, 1996), at 152. *See* AR (Vol. 526 Ref. 95).

broadening the definition of "drug" to include products that affect the structure or function of the body. Congress was concerned not so much with the weight-reduction effects of weight loss products but with the serious and undesirable harms to health that resulted from their use. *See, e.g., Hearing on H.R. 6906, H.R. 8805, H.R. 8941, and S. 5 Before a Subcomm. of the House Comm. on Interstate and Foreign Commerce*, 74th Cong., 1st Sess. 55 (1935) (statement of FDA Chief Walter Campbell), *reprinted in* 4 Legislative History 370.

5. Some comments state that FDA's determination that cigarettes and smokeless tobacco are "drugs" and "devices" would obligate the Agency to regulate caffeine and caffeine-containing products as drugs or drug delivery devices. These comments assert that for this reason the Agency should not regulate tobacco products as drugs or devices. The Agency disagrees that a comparison to caffeine provides a reason not to regulate nicotine-containing cigarettes and smokeless tobacco.

Caffeine is the active ingredient in several products regulated as drugs by the Agency. For instance, caffeine is the active ingredient in NoDoz, an over-the-counter stimulant that is regulated for its effects on the structure and function of the body. Caffeine is also an ingredient in internal analgesics and menstrual discomfort relief products.

Although these products are regulated as drugs, the effects of these caffeine-containing products on the structure and function of the body are significantly less than those of nicotine. *See* section II.A.3.c.i., below. For instance, unlike nicotine, caffeine is not recognized at this time as an addictive drug by health organizations such as the

I.B.

American Psychiatric Association or the World Health Organization. Indeed, even an internal Philip Morris report comparing smoking and caffeine found that nicotine has a stronger stimulant effect than caffeine and that the stimulant effects of caffeine are "more like those of . . . placebo" than of nicotine.[21] The implication for nicotine-containing cigarettes and smokeless tobacco is clear: if caffeine in products such as NoDoz "affect[s] the structure or any function of the body within the meaning of the Act," then *a fortiori* nicotine-containing cigarettes and smokeless tobacco "affect the structure or any function of the body" as well.

Caffeine naturally occurs in coffee, tea, and other foods, and is used as an ingredient in soft drinks. The Act defines "food" as "articles used for food or drink for man or other animals." *See* section 201(f)(1) of the Act, 21 U.S.C. 321(f)(1). The statutory definition "includes articles used by people in the ordinary way most people use food—primarily for taste, aroma, or nutritive value." *Nutrilab v. Schweiker*, 713 F.2d 335, 338 (7th Cir. 1983). When caffeine is used in soft drink products in accordance with section 402 of the Act, 21 U.S.C. 342, and when it naturally occurs in other products that are foods, such as coffee, the product is a "food" under section 201(f)(1) of the Act, 21 U.S.C. 321(f)(1), and is explicitly excepted from the definition of drug in section 201(g)(1)(C), 21 U.S.C. 321(g)(1)(C) ("articles, *other than food*, intended to affect the structure or any function of the body") (emphasis added). The Agency's treatment of caffeine in beverages consequently has no bearing on how cigarettes and smokeless tobacco should be regulated.

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[21] Memorandum from Schori TR to Dunn WL, *Smoking and Caffeine: A Comparison of Physiological Arousal Effects* (May 17, 1972), at 1-2. *See* AR (Vol. 15 Ref. 189-7).

6. Several comments assert that if FDA regulates nicotine-containing cigarettes and smokeless tobacco, it must also regulate the nicotine that occurs naturally in food products such as tomatoes, potatoes, eggplant, and cauliflower. The Agency disagrees. As noted above in response 5, section 201(g)(1)(C) specifically excludes from its coverage products that are "foods" under the Act. Tomatoes, potatoes, eggplant, and cauliflower are "foods" within the meaning of the Act because they are "articles used for food . . . for man." *See* section 201(f)(1), 21 U.S.C. 321(f)(1). While these vegetables do contain trace amounts of nicotine, a person would have to consume 206 pounds of tomatoes, 309 pounds of potatoes, 22 pounds of eggplant, or 355 pounds of cauliflower to obtain the same amount of nicotine as in one cigarette.[22] Thus, these products are appropriately regulated as foods.

7. Some comments question whether applying the structure-function provision to nicotine-containing cigarettes and smokeless tobacco might provide precedent for applying the provision to a wide range of products that have effects on the structure or function of the body—including guns and other weapons, products that prevent injury, such as airbags, and chemical sprays used for self-defense or law enforcement purposes.

The Agency has never construed the structure-function provision to include products such as guns, airbags, and chemical sprays, and applying the structure-function provision to nicotine-delivering tobacco products will not provide any precedent for doing

[22] Chart Y, prepared in conjunction with the testimony of David Kessler before the Subcommittee on Health and the Environment, Committee on Energy and Commerce, U.S. House of Representatives (Mar. 25, 1994). *See* AR (Vol. 296 Ref. 4175).

I.B.

so. Moreover, there are fundamental distinctions between these products and nicotine-delivering tobacco products. Cigarettes deliver a pharmacologically active dose of the drug nicotine to the body through inhalation. Smokeless tobacco delivers a pharmacologically active dose of the same drug through buccal absorption. Collectively, tobacco products achieve their effects on the structure and function of the body through nicotine's pharmacological effects. These include sedation, stimulation, weight control, and maintenance of addiction. Tobacco products are thus indistinguishable from products that the Agency has traditionally regulated as drugs and devices. In contrast, guns, airbags, and chemical sprays are markedly different and distinguishable from such products.

II. CIGARETTES AND SMOKELESS TOBACCO ARE "INTENDED" TO AFFECT THE STRUCTURE AND FUNCTION OF THE BODY WITHIN THE MEANING OF THE ACT

Cigarettes and smokeless tobacco clearly "affect the structure or any function of the body." The principal issue before the Food and Drug Administration (FDA) is thus whether these effects are "intended" within the meaning of the Federal Food, Drug, and Cosmetic Act (the Act).

The Act's drug and device definitions provide in pertinent part that an article is a drug or device if it is "*intended* to affect the structure or any function of the body." Sections 201(g)(1)(C) and 201(h)(3), 21 U.S.C. 321(g)(1)(C) and (h)(3) (emphasis added). In determining whether an article is "intended" to affect the structure or function of the body, "the FDA is not bound by the manufacturer's subjective claims of intent," but rather can find actual intent "on the basis of objective evidence." *National Nutritional Foods Ass'n (NNFA) v. Mathews*, 557 F.2d 325, 334 (2d Cir. 1977). That is, the Agency determines the intent of the manufacturers objectively by evaluating all of the relevant evidence in the record from the perspective of a reasonable fact finder. *See* 21 CFR 201.128, 801.4. In determining intended use, the Agency may "examine a wide range of evidence." *United States v. Two Plastic Drums . . . Black Currant Oil*, 761 F. Supp. 70, 72 (C. D. Ill. 1991), *aff'd*, 984 F.2d 814 (7th Cir. 1993).

In the Jurisdictional Analysis, 60 FR 41453–41787, the Agency determined, based on the evidence then available to it, that cigarettes and smokeless tobacco are "intended" to affect the structure and function of the body. This determination was based on three grounds:

II.

(1) The addictive, psychoactive, and other significant pharmacological effects of cigarettes and smokeless tobacco are so widely known and foreseeable that these effects may be deemed to have been intended by the manufacturers, *see* Jurisdictional Analysis, 60 FR 41483–41490;

(2) Such a large percentage of consumers use cigarettes and smokeless tobacco to satisfy their addiction or to obtain other pharmacological effects that the manufacturers may be deemed to intend that their products will be used for such purposes, *see* Jurisdictional Analysis, 60 FR 41490–41491; and

(3) The statements, research, and actions of the tobacco manufacturers show that the manufacturers actually intend their products to affect the structure or any function of the body, *see* Jurisdictional Analysis, 60 FR 41491–41520.

FDA received comments on its findings from the tobacco industry, public health organizations, and other interest groups and members of the public.

In this section, the Agency considers, in light of the public comments, the objective evidence in the administrative record relevant to whether cigarette and smokeless tobacco manufacturers intend their products to affect the structure or any function of the body, including new evidence that has become available since the issuance of the Jurisdictional Analysis. The Agency also discusses the legal standard for establishing the intended use of cigarettes and smokeless tobacco, and responds to the substantive comments received by the Agency on the evidence and the legal standard. Specifically:

- Section II.A. discusses the evidence supporting FDA's finding that it is foreseeable to a reasonable tobacco manufacturer that the nicotine in cigarettes and smokeless tobacco will cause pharmacological effects and will be used by consumers for those effects and responds to comments on this issue;

II.

- Section II.B. discusses the evidence supporting FDA's finding that consumers use cigarettes and smokeless tobacco predominantly to obtain the pharmacological effects of nicotine and responds to comments on this issue;
- Section II.C. discusses the evidence supporting FDA's finding that cigarette manufacturers' statements, research, and actions show that they intend their products to be used for the pharmacological effects of nicotine and responds to comments on this issue;
- Section II.D. discusses the evidence supporting FDA's finding that smokeless tobacco manufacturers' statements, research, and actions show that they intend their products to be used for the pharmacological effects of nicotine and responds to comments on this issue;
- Sections II.E. and F. respond to comments, not already addressed in the foregoing sections, on the legal standard for evaluating intended use; and
- Section II.G. discusses the cumulative evidence of intended use.

Except as modified below, FDA confirms its prior findings and incorporates them by reference. FDA concludes that the evidence on the foreseeability of nicotine's effects, actual consumer use of tobacco for those effects, and evidence of intended use based on industry statements, research, and actions each provides an independent basis for the determination that the manufacturers of cigarettes and smokeless tobacco intend their products to affect the structure of function of the body.

Although the evidence thus provides several independent bases for establishing that cigarettes and smokeless tobacco are intended to affect the structure and function of the body, the Agency also looks at the objective evidence of intent as a whole. The